

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 7

STATUS OF CLAIMS

Claims 1-29 are pending in the application. Claims 15 and 19-29 have been withdrawn pursuant to a restriction requirement. Thus, claims 1-14 and 16-18 are presently under examination. Claim 1 has been amended. Support for the amendment to claim 1 is provided in the application as filed, e.g., paragraph [0036] of the specification. Claim 14 has been cancelled. Applicants state that the amendment does not present an issue of new matter.

REMARKS

Provisional Double Patenting Rejection

In the Office Action, the Examiner rejected claims 1-14 and 16-18 on the ground of non-statutory obviousness-type double patenting as unpatentable over claims 1-23 of U.S. Patent Application No. 10/894,400, claims 1-14 and 16-18 of U.S. Patent Application No. 10/632,008 and claims 1-14 and 16-18 of U.S. Patent Application No. 10/409,358.

In response, Applicants respectfully traverse the non-statutory obviousness-type double patenting rejection and its accompanying remarks. Applicants also respectfully state that the instant double patenting rejections will be addressed if and when the "provisional" non-statutory obviousness-type double patenting rejection in each application is the only rejection remaining in that application. Pursuant to MPEP 804 I B,

If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Thus, since the co-pending applications have not issued as patents and the claims may be amended in the future, Applicants respectfully exercise their right to address the provisional rejections at a future date, if and when the cited applications are issued as patents.

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 8

Rejection Under 35 U.S.C. § 102(b)

Claims 1 and 4-9 were rejected as being anticipated by Phan et al. (U.S. Pat. No. 5,674,242). Specifically, the Examiner asserts that Phan et al. does not, as claimed, teach away from the inherency required to support the anticipation rejection.

In response, Applicants respectfully traverse the rejection and their accompanying remarks. Phan et al. does not teach all of the elements of the claims, as amended, either explicitly or inherently. For a reference to anticipate a claim it must disclose each and every element of the claim. See MPEP 2131 and cases cited therein, *especially Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) and *In re Marshall*, 578 F.2d 301, 304, 198 USPQ 344, 346 (Fed. Cir. 1978).

Applicants state that Phan et al. fails as an anticipatory reference because it fails to teach all of the claimed elements of the present invention within the four corners of the reference. The invention of claim 1, as amended, is directed to an implantable or insertable medical device comprising (a) a therapeutic agent and (b) a polymeric release region further comprising a polymer selected from the group consisting of homopolymers and copolymers containing polytetrafluoroethylene, collagen, cellulose, polyisobutylene, poly(2-methyl butane), and poly(2-methyl pentene), wherein said polymeric release region is treated with a radiation dose that is effective to substantially increase the cumulative release of said therapeutic agent subsequent to administration to a patient.

Phan et al. does not teach the claimed polymers. Instead, in the Examiner's own words, Phan et al. teach "a methacrylate-containing or an acrylate-containing polymer that is prepared by mixing the monomers methyl methacrylate, polyethyleneglycol methacrylate, and butylmethacrylate in a 2:1.5:1 ratio with a crosslinked, and a thermal or UV initiator (Col. 6, lines 17-27)."

Phan et al. also does not teach irradiating a polymer to increase the cumulative release of the therapeutic agent from the device, or to have any impact whatsoever on the release kinetics of a therapeutic agent from a polymer. Rather, the only instances that radiation is discussed in Phan et al. is for preparing the polymer member, whereby monomers are mixed with a crosslinker to

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 9

polymerize the monomeric mixture into a polymer for extrusion and the extruded tubular structure or flat sheet is then "cross-linked by exposure to UV light, high energy electrons, gamma radiation or heat" (Phan et al., col. 6, lines 21-32; col. 12, lines 60-67 of Example 2). Nowhere does Phan et al. teach utilizing radiation to a finished medical device to substantially increase the cumulative release of a therapeutic agent subsequent to administration to a patient.

Applicants agree with the Examiner's statement that "Phan et al. also teach that the crosslinking occurs by exposure to UV light, high energy electrons, and gamma radiation." However, the Examiner has not met her burden of showing where in Phan et al. there is a teaching or suggestion that such radiation-induced crosslinking leads to the claimed substantial increase in the cumulative release of a therapeutic agent subsequent to administration to a patient. As explained by Applicants in the specification, "[c]rosslinking generally results in the formation of larger, three-dimensional polymer structures."

Phan et al. does not provide any such disclosure or even make such a suggestion. Rather, Phan et al. has explained the effect and function of the crosslinking via a method such as UV radiation, a fact that the Examiner has chosen to ignore: "These polymers can be crosslinked to varying degrees so that the polymer will soften with heat but not flow." (Phan et al., col. 6, lines 14-16).

The Examiner, in essence, believes that it logically follows, that crosslinking a polymer by radiation inherently increases the cumulative release of a therapeutic agent. Applicants disagree.

Radiation is a type of energy that, when applied to polymers, can induce a variety of changes in polymers. The Examiner has offered no evidence to show that irradiation of the polymers of Phan et al., will result in anything more than "crosslink[ing]...so that the polymer will soften with heat but not flow," as taught by Phan et al. (Phan et al., col. 6, lines 14-16).

Applicants reiterate that a holding of inherency must flow as a necessary conclusion from the prior art, not simply a possible one. The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993)

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 10

(reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted); MPEP 2112 IV.

Thus, the fact that the Examiner believes that irradiating the polymers of Phan et al. *may* result in the claimed "substantial[] increase [in] the cumulative release of said therapeutic agent subsequent to administration to a patient," is insufficient to establish inherency.

Thus, Applicants submit that inherency has not been shown and respectfully requests that the Examiner reconsider and withdraw the rejection under 35 U.S.C. 102(b). Even if inherency were to be assumed *arguendo*, the anticipation rejection fails because the four corners of Phan et al. fails to teach the specific polymers claimed.

Claim 1 is the sole independent claim, and the above comments apply directly to this claim. All other rejected claims 4-9 are dependent directly on claim 1 and the rejection of those claims fails at least because of the fundamental defect discussed above.

Rejection under 35 U.S.C. §103(a)

In the Office Action, the Examiner has rejected claims 10-14 and 16-18 under 35 U.S.C. 103(a) as being obvious over Phan et al. in view of Pinchuk (U.S. Pub. No. 2002/0107330) in further view of Furst (U.S. Pub. No. 2002/0099438). Claims 2-3 are rejected as being obvious over Phan et al. in view of Cruise (U.S. Pub. No. 6,537,569).

In response, Applicants respectfully traverse the rejections and their supporting remarks. Applicants state that the Examiner has not met his burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 11

knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) *must teach or suggest all the claimed features*. In addition, the teaching or suggestion to make the claimed combination and the reasonable expectation of success *must both be found in the prior art, not in applicant's disclosure*. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants state that the rejection fails at least because of the fundamental defects discussed above with respect to independent claim 1, as amended, and these defects are not remedied by the secondary references. The prior art references, in combination, fail to teach or suggest all the claim limitations. As indicated above with respect to the anticipatory rejection over Phan et al., Phan et al. fails to teach all of the claimed features, either explicitly or inherently. Neither of the secondary references, Furst, Pinchuk et al. or Cruise, remedies these deficiencies. As such, the Examiner has not established that the combined references teach or suggest all of the claimed features.

Pinchuk et al. teaches nothing of irradiation of polymers, for any purpose. In fact, the words "radiation," and "irradiate" appear nowhere in the disclosures of Pinchuk et al. In view of this deficiency, the Examiner then attempts to connect the materials of Phan et al. to those of Pinchuk et al., by stating that they are equivalent, and thus, it would be obvious to one of skill in the art to apply the radiation taught in Phan et al. to the materials of Pinchuk et al. and such radiation would inherently cause the claimed effect on the respective polymers.

In the Office Action, the Examiner asserts that "[o]ne of ordinary skill in the art would appreciate that methacrylate-containing or an [sic] acrylate-containing polymers and polystyrene-polyisobutylene-polystyrene copolymers are *functional equivalents or one another* making the substitutions in the art obvious variations." (emphasis added). Indeed, she cites Furst, U.S. Pub. No. 2002/0099438, to support this statement. However, nothing in the four corners of Furst, Pinchuk et al., Cruise or Phan et al. supports this theory that the methacrylate and acrylate-containing polymers of Phan et al. are somehow chemical "equivalents" to polystyrene-polyisobutylene-polystyrene (SIBS) copolymers. The Examiner cites to paragraphs [0035],

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 12

[0037], and [0077] of Furst, none of which lend any evidence to this equivalency argument. Furst does not disclose any polystyrene-polyisobutylene-polystyrene copolymers. Furst lists methacrylates and isobutylenes separately in a long listing of candidate materials to “at least partially encapsulate one or more biological agents” or “at least partially form the stent.” (Furst, paragraphs [0035]-[0036]).

Further, Pinchuk et al., invalidates the Examiner’s equivalency claim that “[o]ne of ordinary skill in the art would appreciate that methacrylate-containing or an [sic] acrylate-containing polymers and polystyrene-polyisobutylene-polystyrene copolymers are *functional equivalents or one another* making the substitutions in the art obvious variations.” (emphasis added). Pinchuk et al. teaches that methacrylate-containing polymers are used to form SIBS copolymers, which are very different from the methacrylate starting materials. Indeed, the thrust of the disclosures of Pinchuk et al. is to teach SIBS polymers, a class of polymers with chemical and physical characteristics far superior and different from its components. The components are “soft elastomeric” isobutylene polymers and “hard thermoplastic blocks” made of “monomers of methacrylates or polymers of vinyl aromatics.” (Pinchuk et al., paragraphs [0033] to [0040]). The hard thermoplastic blocks, such as the methacrylate-containing materials, when combined with soft isobutylene-containing blocks, “are capable, inter alia, of altering or adjusting the hardness of the resulting copolymer to achieve a desired combination of qualities.” Pinchuk et al. provides in great detail the polymer chemistry utilized to achieve SIBS materials that have superior drug release characteristics as well as “good biocompatibility” and “good mechanical integrity.” (Pinchuk et al., paragraphs [0018] to [0022]; *see* [0044] to [0058]).

Nothing in Cruise removes the deficiency of the Phan et al. reference. Like Phan et al., Cruise teaches irradiating a polymer in order to cause the crosslinking of polymer chains at free radical sites to form “hydrogels” (Cruise, col. 1, line 59 to col. 2, line 8). Cruise does not teach the claimed polymers. Cruise also does not teach irradiating a polymer to increase the cumulative release of the therapeutic agent from the device, or to have any impact whatsoever on the release kinetics of a therapeutic agent from a polymer.

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 13

Not only is there a lack of explicit teaching of the combination, there is simply no motivation for one of ordinary skill to combine these references. None of the references provides a reason or suggestion to combine the references to arrive at the present invention. *In re Nilssen*, 851 F.2d. 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988). Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006), *cited with approval in, KSR Int'l v. Teleflex, Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ 1385, 1396 (2007). Applicants submit that the Examiner has failed to articulate a rational basis for why a person of skill in the art would combine the references in the manner indicated.

Thus, to make such a combination and make a conclusion of obviousness could only be based on the use of undue hindsight, which has long been held to be impermissible. See, for example, *Akso N.V. v. U.S. International Trade Commission*, 808 F.2d 1241, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987); *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985).

Given the above remarks and the amendments to the claims, Applicant states that the Examiner's rejection under 35 U.S.C § 103(a) has been obviated and Applicant respectfully requests that the Examiner withdraw the rejections.

CONCLUSION

Applicants submit Claims 1-13 and 16-18 are in condition for allowance, early notification of which is earnestly solicited. Should the Examiner be of the view that an interview would expedite consideration of this Amendment or of the application at large, request is made that the Examiner telephone the Applicants' attorney at (908) 518-7700 in order that any outstanding issues be resolved.

FEES

The Examiner is authorized to charge the petition fee for a three-month extension of time and any other fees deemed to be owing for this application to Deposit Account Number 50-1047.

USSN: 10/632,054
Group Art Unit: 1614
Examiner Alicia R. Hughes
Page 14

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